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4	Akabas et al., "A Bitter Substance Induces a Rise in Intercellular Calcium in a Subpopulation of Rat Taste Cells," Science 242:1047-1050 (1988)					in a					
		15		Asano-Miyoshi et al., "Co-Expression of Calcium Signaling Components in Vertebrate Taste Bud Cells," Neurosci. Lett. 283:61-64 (2000)							
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Date

Examiner Signature

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		OTHER PRIOR ART - NON PATENT LITERATURE DOCUMENTS	
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86	30	Fleig et al., "Emerging Roles of TRPM Channels," in "Mammalian TRP Channels as Molecular Targets," Novartis Foundation Symposium 258, John Wiley & Sons, Ltd. pp.248-266 (2004)	
	31	GenBank Accession No. AC003693 (September 30, 1998)	
	32	GenBank Accession No. AF177473 (January 20, 2000)	
	33	Gilbertson et al., "The Molecular Physiology of Taste Transduction," Curr. Opin. Neurobiol. 10:519-527 (2000)	
	34	Gill et al., "Flux Assays in High Throughput Screening of Ion Channels in Drug Discovery," Assay and Drug Dev. Tech. 1(5):709-717 (2003)	
	35	Gordon, J.W., "Transgenic Animals," Intl. Rev. Cytol. 115:171-229 (1989)	
	36	Herness, M.S., "Cellular Mechanisms of Taste Transduction," Ann. Rev. Physiol. 61:873-900 (1999)	
	37	Hofmann et al., "TRPM5 is a Voltage-Modulated and Ca ²⁺ -Activated Monovalent Selective Cation Channel," Current Biol. 13:1153-1158 (2003)	
	38	Hoon et al., "Putative Mammalian Taste Receptors: A Class of Taste-Specific GPCRs with Distinct Topographic Selectivity," Cell 96:541-551 (1999)	
	39	Houghten et al., "Generation and Use of Synthetic Peptide Combinatorial Libraries for Basic Research and Drug Discovery," Nature 354:84-86 (1991)	
	40	Huang et al., "Gy13 Colocalizes with Gustducin in Taste Receptor Cells and Mediates IP ₃ Responses to Bitter Denatonium," Nat. Neurosci. 2(12):1055-1062 (1999)	
100	41	Huston et al., "Protein Engineering of Antibody Binding Sites: Recovery of Specific Activity in an Anti-Digoxin Single-Chain Fv Analogue Produced in Escherichia coli," Proc. Natl. Acad. Sci. USA 85:5879-5883 (1988)	

Examiner Signature	Date Considered	(0-20-05

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8	42	Kinnamon & Margolskee, "Mechanisms of Taste Transduction," Curr. Opin. Neurobiol. 6(4):506-513 (1996)					
	43	Köhler & Milstein, "Continuous Cultures of Fused Cells Secreting Antibody of Predefined Specificity," Nature 256:495-497 (1975)					
	44	Komuro & Rakic, "In Vitro Analysis of Signal Mechanisms Involved in Neuronal Migration," in L.W. Haynes ed., The Neuron in Tissue Culture, New York: John Wiley & Sons, pp.57-69 (1999)					
	45	Kozbor & Roder, "The Production of Monoclonal Antibodies from Human Lymphocytes," Immunology Today 4(3):72-79 (1983)					
	46	Lakso et al., "Targeted Oncogene Activation by Site-Specific Recombination in Transgenic Mice," Proc. Natl. Acad. Sci. USA 89:6232-6236 (1992)					
	47	Lam et al., "A New Type of Synthetic Peptide Library for Identifying Ligand-Binding Activity," Nature 354:82-84 (1991)					
	48	Lavitrano et al., "Sperm Cells as Vectors for Introducing Foreign DNA into Eggs: Genetic Transformation of Mice," Cell 57:717-723 (1989)					
	.49	Lindemann, B., "Receptors and Transduction in Taste," Nature 413:219-225 (2001)					
	50	Lindemann, B., "Taste Reception," Physiological Reviews 76(3):719-766 (1996)					
	51	Liu & Liman, "Intracellular Ca ²⁺ and the Phospholipid PIP ₂ Regulate the Taste Transduction Ion Channel TRPM5," PNAS 100(25):15160-15165 (2003)					
	52	Lo, C.W., "Transformation by Iontophoretic Microinjection of DNA: Multiple Integrations Without Tandem Insertions," Mol. Cell Biol. 3(10):1803-1814 (1983)					
	53	McLaughlin et al., "Gustducin is a Taste-Cell-Specific G Protein Closely Related to the Transducins," Nature 357:563-569 (1992)	-				
8	54	Ming et al., "Blocking Taste Receptor Activation of Gustducin Inhibits Gustatory Responses to Bitter Compounds," <i>Proc. Natl. Acad. Sci. USA</i> 96:9903-9908 (1999)					

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8	Ming et al., "Characterization and Solubilization of Bitter-Responsive Receptors That Couple to Gustducin," <i>Proc. Natl. Acad. Sci USA</i> , 95:8933-8938 (1998)		
	56	Montell, C., "New Light on TRP and TRPL," Mol. Pharmacol. 52:755-763 (1997)	
	57	Morrison et al., "Chimeric Human Antibody Molecules: Mouse Antigen-Binding Domains with Human Constant Region Domains," Proc. Natl. Acad. Sci. USA 81:6851-6855 (1984)	
	58	Neuberger et al., "Recombinant Antibodies Possessing Novel Effector Functions," Nature 312:604-608 (1984)	
	59	Ninomiya et al., "Lack of Gurmarin Sensitivity of Sweet Taste Receptors Innervated by the Glossopharyngeal Nerve in C57BL Mice," Am. J. Physiol. 272(3 Pt 2):R1002-1006 (1997)	
	60	Perez et al., "A Transient Receptor Potential Channel Expressed in Taste Receptor Cells," Nature Neurosci. 5(11):1169-1176 (2002)	
	61	Prawitt et al., "Identification and Characterization of MTR1, A Novel Gene With Homology to Melastatin (MLSN1) and the trp Gene Family Located in the BWS-WT2 Critical Region on Chromosome 11p15.5 and Showing Allele-Specific Expression," Human Molecular Genetics, 9(2):203-216 (2000)	
	62	Ruiz-Avila et al., "Coupling of Bitter Receptor to Phosphodiesterase Through Transducin in Taste Receptor Cells," Nature 376:80-85 (1995)	
	63	Sambrook et al., "Molecular Cloning," 2 nd Ed. Cold Spring Harbor Laboratory Press (1989) (Table of Contents only)	
	64	Songyang et al., "SH2 Domains Recognize Specific Phosphopeptide Sequences," Cell 72:767-788 (1993)	
	65	Takeda et al., "Construction of Chimaeric Processed Immunoglobulin Genes Containing Mouse Variable and Human Constant Region Sequences," Nature 314:452-454 (1985)	
70	66	Thompson et al., "Germ Line Transmission and Expression of a Corrected HPRT Gene Produced by Gene Targeting in Embryonic Stem Cells," Cell 56:313-321 (1989)	

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OTHER PRIOR ART – NON PATENT LITERATURE DOCUMENTS								
Examiner Initials	Cite No.1							
565	67	van der Putten et al., "Efficient Insertion of Genes Into the Mouse Germ Line Via Retroviral Vectors," <i>Proc. Natl. Acad. Sci. USA</i> 82:6148-6152 (1985)						
	68	Ward et al., "Binding Activities of a Repertoire of Single Immunoglobulin Variable Domains Secreted from Escherichia coli," Nature 341:544-546 (1989)						
	69	Wolff et al., "Comparative Study of Membrane Potential-Sensitive Fluorescent Probes and Their Use in Ion Channel Screening Assays," J. Biomol. Screening 8(5):533-543 (2003)						
S	70	Xu et al., "Ion-Channel Assay Technologies: quo vadis?," Drug Discov. Today 6(24):1278-1287 (2001)						

			
Examiner Signature	44	Date Considered	6-20-05

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